THE ULTIMATE RESIDUAL LESIONS OF ASPHYXIA NEONATORUM

WITH THREE CASES OF PORENCEPHALY

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The aetiology of the degenerative brain conditions of infants and children is as yet not fully understood. Congenital and infective causes, as well as birth injuries, are recognized as important causes, but it is only recently that the role played by anoxia as an aetiological factor is becoming more fully realized. The majority of these brain lesions have been caused experimentally by exposing laboratory animals to anoxia. Furthermore, in many cases of degenerative brain conditions which are diagnosed clinically or at post-mortem examination, a history of asphyxia neonatorum is obtained; in one series of cases,[13] a history of apnoea at birth was obtained in 70% of 500 children with neurological abnormalities. As is well known, anoxia may cause cerebral palsy and, as Evans [6] believes, usually of the athetotic type.

CONDITIONS WHICH MAY BE CAUSED BY ASPHYXIA NEONATORUM

I. Courville [2] divides these results into 4 groups:

1. *Diffuse Loss of Nerve Cells.* In this condition there is, according to Courville, such a diffuse loss of nerve cells that the convolutions of the brain are smaller than normal, but there are no recognizable changes in the internal structure. Experiments [17] were carried out in which the uterine arteries of gravid guinea-pigs were temporarily occluded, and the subsequent progeny showed either localized or diffuse atrophy of the brain cortex as the result of generalized loss of nerve cells. The corpus striatum is also extremely sensitive to anoxia and Courville is of the opinion that this is an important cause of juvenile Parkinsonism and congenital choreo-athetosis.

2. *Cortical Sclerosis, generalized or localized.* In this condition atrophy and sclerosis of the convolutions result and this may be generalized or localized. Courville[2] quotes a case in which Meyer found atrophic nodes of the cortex at the post-mortem examination of a patient who 16 years previously had suffered from carbon-monoxide poisoning—the obvious cause of the anoxia. He supposes that the formation of scar tissue in the cortex, following exposure to anoxia, may eventually lead to epileptiform attacks. This type of lesion has also been found in cases of spastic paralysis of children.

3. *Disorders of Myelination.* Encephalitis periaxialis diffusa (Schilder's disease) was previously considered to be of inflammatory origin, but this idea has been largely abandoned. In 1926 [8] its similarity to demyelination, which follows on carbon-monoxide poisoning, was noticed. Courville considers asphyxia neonatorum or intra-uterine anoxia to be the most likely cause both of the infantile and the subacute type of Schilder's disease in children.

4. *Cyst-formation and Porencephaly.* In early life 2 other cerebral lesions occur, viz. chronic infantile cystic degeneration and porencephaly. The former condition was at first considered to be of inflammatory origin, but its early association with birth injuries and subdural haematomas pointed to a traumatic origin. This was confirmed by the experimental production of cystic degeneration of the brain as a result of cerebral anoxia caused by inhalation of carbon-monoxide and nitrous oxide.

Perhaps the most widely accepted definition of porencephaly is that of Le Count and Semerak,[18] who describe it as 'a defect communicating with the ventricles or separated from them by a thin layer of brain tissue, and covered on the outside by the arachnoid'. The different aetiological factors causing porencephaly may be classified as developmental, traumatic, vascular and inflammatory. Traumatic and vascular factors are closely interrelated. Vascular accidents such as haemorrhage, embolism and thrombosis may lead to cerebral anoxia, with porencephaly as the result. This has been observed experimentally as well as clinically. Inflammatory lesions such as tuberculosis, syphilis and meningo-encephalitis have been described as underlying causes of porencephaly. 'The very multiplicity of possibilities in many instances makes it difficult to establish the underlying cause.' [18] In a series of 29 cases of Pendergrass and Perryman [18] the aetiology was not definitely determined in 17 cases. Five of their cases were apparently caused by intra-uterine or birth injuries, 3 by trauma in later life and 2 by encephalitis. It is clear that porencephaly may follow neonatal asphyxia, and its recognition is important in determining prognosis and in differentiation from mass-producing or constricting lesions involving the brain. Of their 29 cases 26 sought medical attention because of epileptic attacks, while the others complained of headache, poor memory, irritability and mental retardation. In 2 of our cases the chief complaints were excessive developmental and mental retardation, both with complete blindness and one with repeated convulsions. The 3rd case presented with extreme spasticity.

A definite diagnosis of porencephaly can be made only by the use of pneumo-encephalography, and porencephaly may still be demonstrated by films taken 24 hours after the injection of air into the lumbar subarachnoid space.

II. *Other Effects on the Central Nervous System*

1. *Intelligence.* It is difficult to assess the effect of asphyxia neonatorum on the intelligence. It can be done by obtaining the birth history of the mentally retarded children. Campbell *et al.*[1] point out that a history taken from a mother after the passing of several years may be inaccurate or may be unduly modified in order to give a reason for her child's mental condition. The Darke's studies [4] show that children may well have subnormal intelligence as a result of asphyxia neonatorum. Other

investigators [1, 16] were not able to elicit proof of a greater occurrence of lowered intelligence in these cases as compared with normal controls. The answer will only be found after large series with adequate follow-up investigations have been studied.

2. *Behaviour Disorders.* It is well known that changes in behaviour can occur after the administration of anaesthetics, especially nitrous oxide. This is attributed to anoxia. Fletcher [7] described 27 cases following nitrous oxide anaesthesia. The disturbances may occur early or years afterwards; they may improve within months or over a number of years or may become progressively worse. Amongst others, he noticed the following symptoms: mental confusion, poor concentration and memory, behaviour disorders, apathy, hysteria, restlessness and headache. He believes that the sensitive cortical cells are damaged by the anoxia. The condition may improve in time, but where the damage is extensive the changes may be irreversible. He suggests that repeated administration of anaesthetics to children, and asphyxia neonatorum, may result in behaviour disturbances.

Preston [11] described 132 cases of behaviour abnormalities in children with a history of anoxia at birth. He distinguishes three groups: (*a*) with hyperactive behaviour—37%, (*b*) with apathetic behaviour—34%, and (c) with epileptic behaviour—29%. The intelligence of 35 of the 132 cases was subnormal and the rest normal, but all were problem children.

Rosenfeld and Bradley [12] perused the records of 673 children with abnormal behaviour. In a large percentage a hisotry of apnoea at birth or of pertussis before the age of 3 years was found; the only factor which these two conditions have in common is anoxia.

3. *Epilepsy.* Epilepsy as a late result of anoxia is well known. Preston [11] also mentioned this in his series of cases. Courville [2] believes that anoxia causes cortical sclerosis resulting in epileptic seizures. Nielsen [9] is of the opinion that anoxia is responsible for some cases of idiopathic epilepsy. Instances of epilepsy have been reported in pilots who have flown at great heights with inadequate oxygen supplies.

4. *Hemiplegia.* At the post-mortem examination in a case of a woman aged 80 years with hemiplegia since birth a cyst was discovered in the internal capsule together with widespread degenerative lesions of the brain.[3] These findings indicated anoxia as the causal factor.

5. *Electro-encephalographic changes.* In ECG investigations carried out in Sweden [5] on 61 children who had had asphyxia neonatorum 4 to 7 years previously, 24 (40%) showed abnormal rhythm and low-frequency waves. It is stated that only 5% of normal children shows an abnormal encephalogram, which makes the high percentage in the series significant.

As an example of the late results of antenatal and neonatal asphyxia, three cases are presented where porencephaly was found as the ultimate residual lesion.

CASE 1

A Bantu boy 18 months old was admitted on 8 March 1954 to Professor Davel's paediatric wards. The patient's neck and arms had been flaccid since birth. He was still unable to lift his head or sit or crawl and was incapable of any speech. From birth feeds had been taken with difficulty and growth was retarded.

Birth History. He was the firstborn baby, full term. The confinement at home, without professional aid, was difficult and protracted, labour lasting 2 days. Breathing and crying were absent immediately after birth, cyanosis was extreme and resuscitation unsuccessful, the infant being presumed dead. Two hours later, however, it was noticed that the baby was alive.

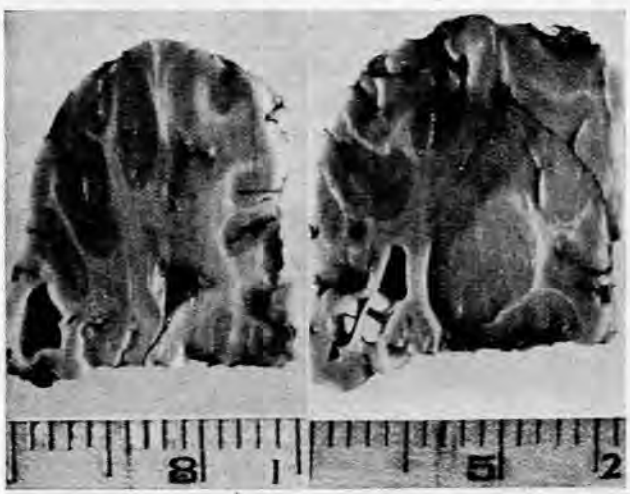
On Examination. The patient was emaciated and underdeveloped; the head was retracted and mouth gaping. Weight 13 lb. 1 oz.; head circumference 17 inches; anterior fontanelle was almost closed.

Central Nervous System. The patient was obviously mentally and physically retarded. The cranial nerves were normal except for an internal strabismus of the right eye. The neck was flaccid, with hypotonia of the arms and decreased tendon reflexes. There was hypertonia of the lower limbs with slight adductor spasm.

No further abnormalities were found in any of the other systems.

Special Investigations. Roentgen photos of the skull were normal except for microcephaly. C.S.F. showed no abnormalities. The blood picture was normal. Before any further investigations could be carried out, the child suddenly developed hyperpyrexia and died.

Post-Mortem Examination. After removal and fixation of the brain, sections showed 2 subcortical cysts in the left frontal region (Figs. 1 and 2). Histological examination of the cortex and basal ganglia (by Prof. J. Barnetson) revealed no obvious changes. No further abnormalities excepting a fatty infiltration of the liver were found.



Figs. 1 *and* 2. Case 1. Sections of the left hemisphere show the 2 subcortical cysts with no communication with the ventricular system. An encephalogram would have been negative in this case.

CASE 2

A European baby-girl 3 months old was admitted to the paediatric wards for the first time on 23 September 1953, suffering from gastro-enteritis. Since then she has been admitted on 3 other occasions with the same complaint. On the 4th admission (2 February 1954) at the age of 7 months, it was noticed for the first time that she was unable to hold her head erect, was not able to sit upright and could not observe objects. Examination revealed a head circumference of 16 inches and commencing bilateral optic atrophy. Roentgen photos of the skull showed no abnormalities but, after 25 c.c. of air had been introduced by the lumbar thecal route, a shadow was demonstrated above and lateral to the right lateral ventricle (Fig. 3). On the last admission (15 September 1954) at the age of 15 months, the head circumference was 16½ inches and complete primary optic atrophy was present. The developmental age at this stage is that of a baby of 2 months. She is not able to keep her head erect or to sit up. The Moro reflex is still present. Special investigations of the blood and C.S.F. gave normal results; the Kolmer reaction was negative.

Antenatal and Birth History. About 2 weeks after the expected menstrual period the mother had a slight vaginal haemorrhage lasting 1 day. A week later she had another haemorrhage lasting 2 days followed 6 weeks later by a severe haemorrhage for which she was admitted to hospital and treated for a threatened abortion. After this everything went well until the 7th month, when she again had a severe haemorrhage and this time was admitted as a suspected placenta praevia. The bleeding subsided and she was sent home again until labour commenced at full term. It was very difficult and lasted several hours. According to the mother, no instruments were used, but the head was manually rotated and a large episiotomy done. The baby was very blue; the blueness lasted for 3 days and gradually disappeared. The birth weight was $5\frac{1}{2}$ pounds.

CASE 3

A 13-month-old Bantu baby-boy was admitted with gastro-enteritis; further history elicited mental and developmental retardation with suspected blindness. A month before admission his left leg became spastic.

Pregnancy history revealed no haemorrhages, illnesses or virus infections. Labour itself was considered to be normal, but this history is usually unreliable with Bantu people.

On examination, the child showed slight dehydration. He was blind and could neither keep his head erect or sit up. The Moro reflex was still present and the left leg was slightly spastic. His head circumference was 16 inches and he was completely blind, with complete optic atrophy. Special examinations of the blood and C.S.F. were normal, with negative Kolmer tests. A pneumo-encephalogram revealed porencephaly (Fig. 4).

Comment. In the first case prolonged asphyxia neonatorum obviously caused severe anoxia with the results stated. In case 2 there was an additional history of antenatal haemorrhage and one wonders what influence the small bleedings in early pregnancy could have had. Case 3 gave no history of any antenatal or neonatal asphyxia, but the baby revealed the same condition as the other two. Pneumo-encephalography showed the porencephaly to be more widespread than in the other two cases.

Discussion: It is now believed that asphyxia neonatorum and antenatal anoxia may have serious residual effects, not only as an immediate, but also as a late complication. Parturition [10] is the most dangerous experience to which the individual is normally subjected and one of the greatest dangers is anoxia. For this reason there are different mechanisms [14, 15] for the protection of the foetus and neonatus against this danger. The most important factor is probably the greater affinity of foetal haemoglobin for oxygen in comparison to that of the adult. Furthermore, the metabolic rate of the brain of the newly-born is low and anaerobic conversion of blood-sugar occurs. Should the apnoea be of long duration, it may give rise to irreparable damage of the sensitive nerve cells with varied resultant clinical entities such as porencephaly, Schilder's disease, cerebral palsy, epilepsy, mental retardation, and others.

In case 1, where anoxia was of long duration, the clinical findings were those of cerebral palsy and this, together with the post-mortem findings of porencephaly,

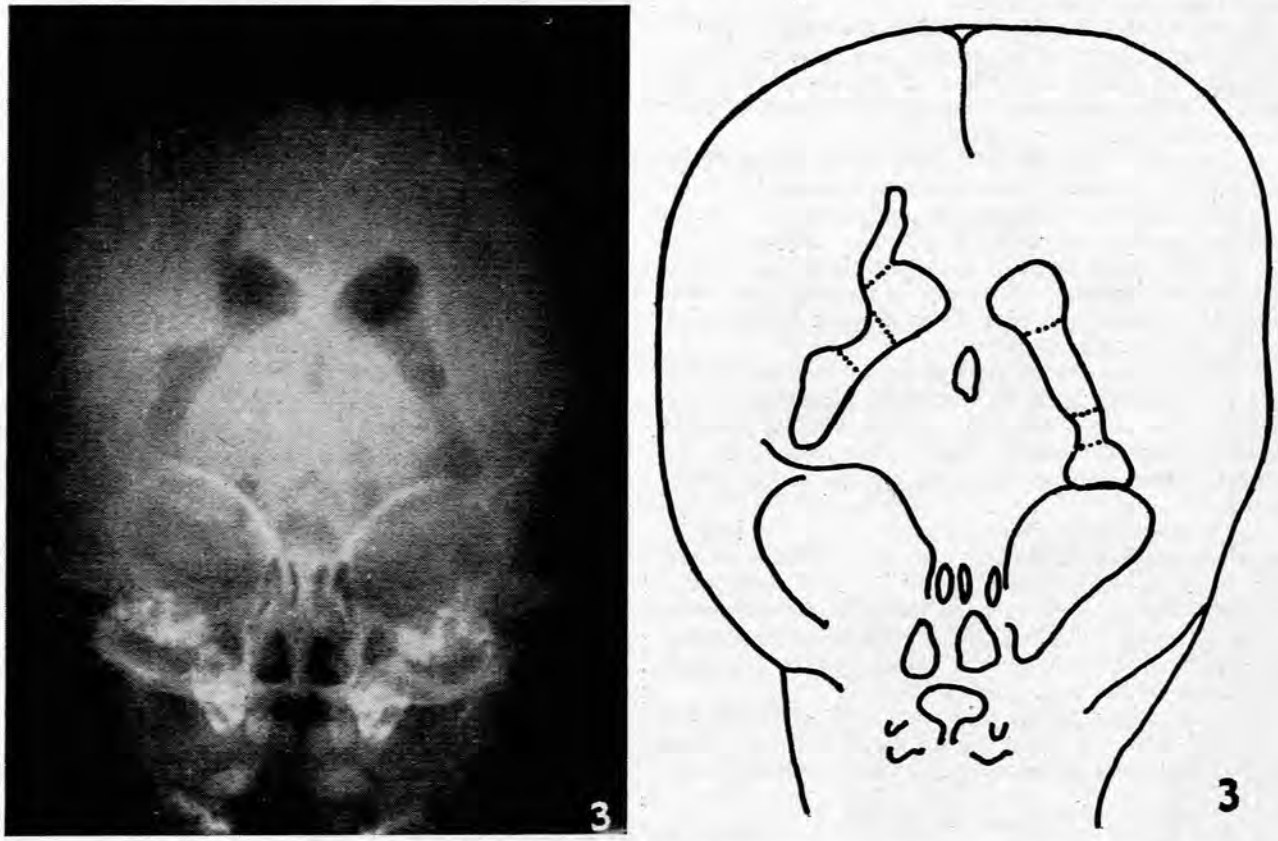
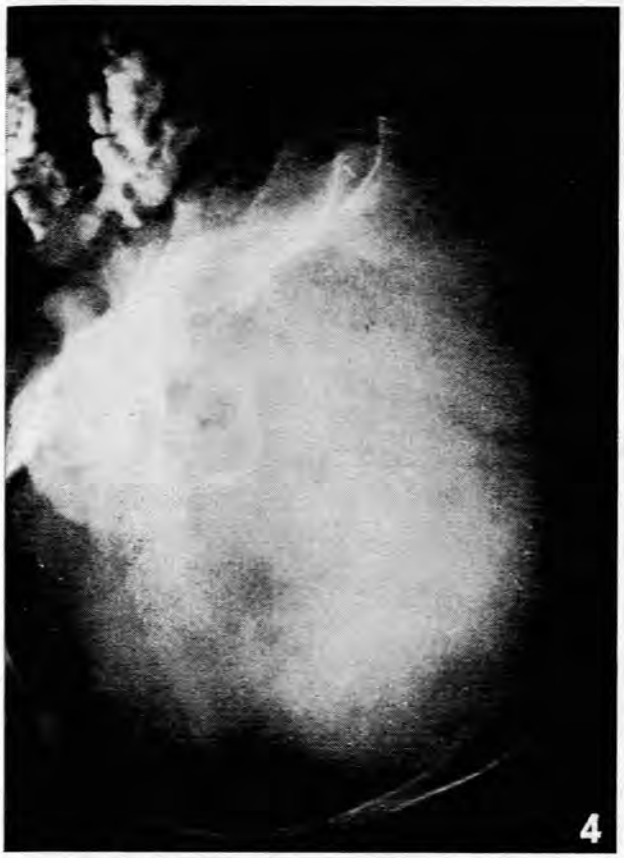


Fig. 3. Case 2. Encephalogram illustrates porencephaly in the left hemisphere communicating with the anterior cornu of the right lateral ventricle. Also diagram of same.



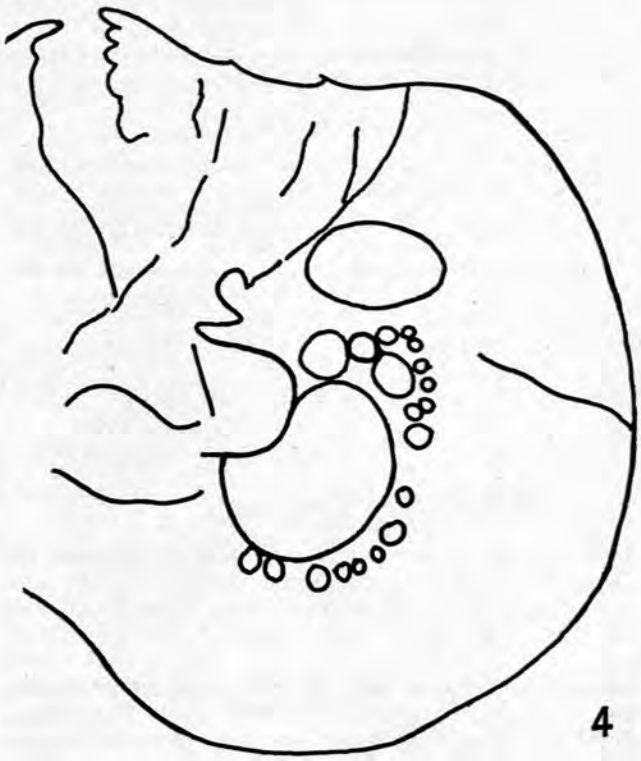


Fig. 4. Case 3. Encephalogram shows a cluster of 'daughter' cysts on the wall of a large 'mother' cyst; this is very rarely seen. Also diagram of same.

are typical ultimate residual lesions of anoxia. There is adequate evidence that anoxia plays an important role in the aetiology of a large group of apparently unrelated degenerative conditions of the central nervous system. Two changes are thought to occur: Firstly, where damage to the nerve cells is minimal, there is every possibility, according to Fletcher,[7] of improvement taking place with the passing of months or years. This was proved by his observations on patients with mental disorders following repeated general anaesthesia. Preston's observations on children with behaviour disorders as a result of neonatal anoxia substantiate this view.[11] Secondly, where the damage is extensive, degenerative brain lesions develop.

Courville supposes that anoxia produces minimal functional changes in the nerve cells which shorten their life-span. The cells, after functioning normally for several years, start deteriorating. Thus symptoms may only occur in later childhood or even during adult life.

SUMMARY

It is now accepted that anoxia (antenatal, natal and postnatal) is a most important single factor in the development of degenerative lesions of the central nervous system in children and probably in adults as well. Conditions such as cerebral palsy, Schilder's disease, porencephaly, epilepsy, juvenile Parkinsonism, etc., may be caused in this manner. Anoxia may likewise be responsible for some behaviour disorders and lowered intelligence in children. Three cases with porencephaly are described, 2 of them following prolonged post-natal and antenatal anoxia. Similar changes caused by asphyxia neonatorum and prenatal anoxia are described in the literature reviewed.

OPSOMMING

Dit word aanvaar dat asphyxia neonatorum, asook prenatale anoksie 'n belangrike rol speel in die etiologie van degeneratiewe breinsiektes van babas, kinders en miskien ook van volwassenes. Toestande soos serebrale verlamming, Schilder se siekte, porenkefalie, epilepsie, Parkinsonisme van jeugdiges ens., mag hierdeur veroorsaak word. Dit mag ook verantwoordelik wees vir gedragsafwykings en lae intelligensie by kinders. Drie gevalle van porenkefalie bewys met pneumo-enkefalografiese ondersoeke en lykskouing word beskryf. In 2 gevalle is daar 'n duidelike geskiedenis van prenatale en postnatale anoksie. Die kliniese verskynsels van hierdie drie gevalle het bestaan uit geestelike en liggaam-

like agterlikheid, mikrokefalie, optiese atrofie en serebrale verlamming.

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